

Applicant : Shawn Shui-On Leung
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Amendments to the claims:

1-39. (Canceled)

40. (Currently amended) A ~~re-engineered, or~~ framework (FR)-patched immunoglobulin ~~containing a heavy or light or heavy and light variable regions sequences from a parent antibody, in which~~ , wherein at least one or more of the compartmentalized framework sequences, defined as FR1, FR2, FR3 and FR4, of at least one heavy or light chain are replaced, ~~or patched by the corresponding compartmentalized framework sequences from the heavy or light or heavy and light chain immunoglobulin variable region of a different species or from a different immunoglobulin of the same species, respectively, wherein said re-engineered immunoglobulin comprises compartmentalized framework sequences from at least two different sources of different immunoglobulin chains, wherein said different immunoglobulin chains can be sourced from different immunoglobulins of the same species, or from different immunoglobulins of different species, and such re-engineered FR-patched immunoglobulin binds specifically to an antigen with affinity within 3-fold of that of the parent immunoglobulin, with the proviso that not all of the replaced FR1, FR2 and FR3 of the re-engineered a FR-patched immunoglobulin heavy chain are from the same framework of a single immunoglobulin heavy chain, and not all the replaced FR1, FR2 and FR3 of the re-engineered a FR-patched immunoglobulin light chain are from the same framework of a single immunoglobulin light chain.~~

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41. (Currently amended) A re-engineered or FR-patched immunoglobulin according to Claim 40, in which the particular FR chosen for patching or replacing each corresponding FR in the parent immunoglobulin:

- a. exhibits the highest degree of homology, or at least 60%, to the corresponding parent FR;
- b. exhibits identical sequence homology to the corresponding parent FR at the three amino acids immediately adjacent to the flanking CDR's; and
- c. contains identical amino acid to the corresponding parent FR at positions known to be close to, or have interactions with the CDR's/antigen binding site, as evaluated by computer modeling, crystal structure, or published information, ~~or prior experience~~.

42. (Currently amended) A re-engineered, or FR-patched immunoglobulin according to Claim 40, in which the particular FR chosen for patching or replacing each corresponding FR in the parent immunoglobulin:

- a. exhibits the highest degree of homology, or at least 60%, to the corresponding parent FR;
- b. exhibits identical sequence homology to the corresponding parent FR at the four amino acids immediately adjacent to the flanking CDR's; and

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c. contains identical amino acid to the corresponding parent FR at positions known to be close to, or have interactions with the CDR's/antigen binding site, as evaluated by computer modeling, crystal structure, or published information, ~~or prior experience~~.

43. (Currently amended) A re-engineered or FR-patched immunoglobulin according to Claim 40, in which the particular FR chosen for patching each corresponding FR in the parent immunoglobulin:

a. exhibits the highest degree of homology, or at least 60%, to the corresponding parent FR;

b. exhibits the highest degree of sequence homology to the corresponding parent FR, preferably identical, or contains conservatively similar amino acids at the four amino acids immediately adjacent to the flanking CDR's; and

c. contains identical, or conservatively similar amino acids to the corresponding parent FR at positions known to be close to, or have interactions with the CDR's/antigen binding site, as evaluated by computer modeling, crystal structure, or published information, ~~or prior experience~~.

44. (Currently amended) A re-engineered or FR-patched immunoglobulin according to Claim 40, in which the

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particular FR chosen for patching or replacing each corresponding FR in the parent immunoglobulin:

- a. exhibits the highest degree of homology, or at least 60%, to the corresponding parent FR;
- b. exhibits the highest degree of sequence homology to the corresponding parent FR, preferably identical, or contains conservatively similar amino acids at the three amino acids immediately adjacent to the flanking CDR's; and
- c. contains identical, or conservatively similar amino acids to the corresponding parent FR at positions known to be close to, or have interactions with the CDR's/antigen binding site, as evaluated by computer modeling, crystal structure, or published information, ~~or prior experience.~~

45. (Current amended) A ~~re-engineered, or~~ FR-patched immunoglobulin according to claim 40, ~~containing the heavy or light or heavy and light chain variable region sequences from a parent antibody, in which the particular FR chosen for patching each corresponding FR in the parent immunoglobulin comprises amino acids derived from the parent immunoglobulin framework outside the Kabat and Chothia CDRs, wherein the parent one or more amino acids from said parent immunoglobulin replace corresponding amino acids in the patching FR, wherein the patching FR is the FR derived from a different source used for~~

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~~patching, or that replaces the original FR of, the parent immunoglobulin~~ one or more of said donor immunoglobulin sequences.

46. (Previously presented) A re-engineered, or FR-patched immunoglobulin according to Claim 40, which specifically binds to an antigen with an affinity of between 10^7 M^{-1} and 10^{11} M^{-1} .
47. (Previously presented) A re-engineered, or FR-patched immunoglobulin according to Claim 40, which specifically binds to an antigen with an affinity of between 10^8 M^{-1} and 10^{10} M^{-1} .
48. (Previously presented) A re-engineered or FR-patched immunoglobulin according to Claim 40, which is substantially pure.
49. (Previously presented) A pharmaceutical composition comprising a re-engineered or FR-patched immunoglobulin according to Claim 40, in a pharmaceutically acceptable carrier.
50. (Canceled)